Esophageal Cancer Among Black Men in Washington, D.C. II. Role of Nutrition [1]

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ABSTRACT—A case-control study of esophageal cancer was conducted among the black male residents of Washington, D.C., to find reasons for the exceptionally high risk in this population. The next of kin of 120 esophageal cancer cases who died during 1975-77 and of 250 D.C. black males who died of other causes were interviewed. Five indicators of general nutritional status—fresh or frozen meat and fish consumption, dairy product and egg consumption, fruit and vegetable consumption, relative weight (wt/ht^2), and number of meals eaten per day—were each significantly and inversely correlated with the relative risk of esophageal cancer. Associations with other food groups were not apparent. The least nourished third of the study population, defined by any of these five measures, was at twice the risk of the most nourished third. None of these associations was markedly reduced by controlling for ethanol consumption, the other major risk factor in this population; smoking; socioeconomic status; or the other nutrition measures. When the three food group consumption measures were combined into a single overall index of general nutritional status, the relative risk of esophageal cancer between extremes was 14. Estimates of the intake of vitamin A, carotene, vitamin C, thiamin, and riboflavin were inversely associated with relative risk; but each micronutrient index was less strongly associated with risk than were the broad food groups that provide most of the micronutrient. Thus no specific micronutrient deficency was identified. Instead, generally poor nutrition was the major dietary predictor of risk and may partially explain the susceptibility of urban black men to esophageal cancer.—JNCI 1981; 67:1199-1206.

A case-control study of esophageal cancer was initiated among black male residents of Washington, D.C., the U.S. metropolitan area with the highest esophageal cancer mortality rate for nonwhite males for 1970-75 (*1*). In an earlier paper, alcoholic beverage consumption was identified as the dominant risk factor; but poor nutrition was also implicated (*1*). In the present paper the role of nutritional status in esophageal cancer is further assessed.

MATERIALS AND METHODS

The 120 cases in the study were all black male residents of Washington, D.C., who died during 1975-77 of primary esophageal cancer [code No. 150 (*2*)]. The 250 controls were randomly selected from among D.C. black males of the same age who died of other causes during the same time period, after oral, pharyngeal, and laryngeal cancer were excluded. Next of kin were identified from the death certificates and interviewed in 1979 about the dietary patterns, cooking practices, alcohol consumption, and tobacco use of the study subjects. Interviews were completed for 67% of the cases and 71% of the controls. The next of kin interviewed were wives (45%, 45%), other relatives (48%, 48%), and friends (6%, 7%) for the cases and controls (respectively). Further details are given elsewhere (*1*). An earlier attempt to interview esophageal cancer patients directly had floundered because of the small number of incident cases that could be prospectively identified and the advanced disease in these patients once located.

The dietary section of the interview asked about the usual adult frequency of consumption, prior to 1974, of 31 food items. Answers were converted to the number of times a food item was eaten per week. To explore the basic dietary patterns associated with esophageal cancer, measures of consumption of food groups were created by summing responses for individual food items. Traditional food groups, such as green vegetables, fruit, and meat-fish, were formed, as well as less traditional groups, such as nitrite-containing foods (bacon, frankfurters, lunch meat, corned beef-pastrami, and canned meat). Beef, chicken, lamb, fresh or frozen fish, and shellfish were combined into a food group of relatively "affluent" foods called "fresh or frozen meat and fish"; and frankfurters, lunch meat, canned meat, canned fish, bacon, and sausage were combined into a food group of generally cheaper foods called "precooked or processed meat and fish."[4]

Indices of micronutrient intake for vitamin A, carotene, vitamin C, thiamin, and riboflavin were created

ABBREVIATIONS USED: fl oz = fluid ounce(s); kcal = kilocalorie(s); RR = relative risk(s).

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[4] Four meats did not clearly belong in one or the other of these 2 subgroups and were excluded from both: liver, pastrami-corned beef, brains-chitterlings, and ham-pork. The interview question about ham-pork was considered ambiguous since chops and pigs' feet had been given as examples. The "precooked or processed meat and fish" group was referred to as the "precooked or cured meat and fish" group in the earlier paper (*1*).

by weighting and summing responses for the appropriate individual food items. Each weight was the quantity of the micronutrient in a typical serving of the food item and was derived from U.S. Department of Agriculture food composition data (*3, 4*). To form the vitamin A index, carotene- and retinol-containing foods were weighted according to the number of retinol equivalents that they contain (*5*).

Five cases (4%) and 25 controls (10%) were excluded from all the dietary analyses because few of the food frequency questions could be answered by their next of kin. The remaining next of kin of the cases and of the controls could both answer quantitatively an average of 96% of the food frequency questions. To form the food group and micronutrient variables, any response in which it was not known whether an individual food item was eaten was coded as "0"; and any response in which a food item was known to be eaten but with unknown frequency was replaced with the study sample median, which was calculated after nonconsumers had been eliminated from the distribution. Three consumption categories—low, moderate, and high—were created for each food item, food group, and micronutrient index by dividing the frequency distribution of the variable into approximate thirds.

A simple measure of relative weight was formed by dividing usual adult weight (prior to 1974), in pounds, by the square of adult height, in feet. The study sample was divided into four strata on the basis of ideal and typical relative weights for this population: those lighter than ideal ($wt/hr^2 \leq 4.32$), those centered around the ideal relative weight ($4.32 < wt/ht^2 \leq 4.84$), those centered around the typical relative weight ($4.84 < wt/ht^2 \leq 5.72$), and those heavier than typical ($wt/ht^2 > 5.72$). An ideal relative weight of 4.52 was derived from the National Academy of Sciences Food and Nutrition Board's recommendation for adult men (*5*). A median or typical relative weight of 5.04 was calculated from data obtained for black males, 55-64 years of age, in the 1971-74 U.S. Health and Nutrition Examination Survey (*6*).

Usual alcoholic beverage consumption was measured in terms of grams of ethanol and calories. Total ethanol intake was calculated by summing the intake of beer (1.1 g ethanol/fl oz), wine (2.9 g ethanol/fl oz), and hard liquor (9.4 g ethanol/fl oz) (*3*). Total calorie intake was also calculated by summing the intake of beer (13 kcal/fl oz), wine (25 kcal/fl oz), and hard liquor (65 kcal/fl oz) (*3*).

RR were estimated by the odds ratio (*7*), and associations were further examined by calculating odds ratios stratified by various factors, with summary RR estimated by the Mantel-Haenszel method (*8*). Adjustment for ethanol consumption was routinely done over six strata, identified in table 2 of (*1*), and over nine strata for the five primary nutrition indices. Unless otherwise noted, ethanol-adjusted RR presented in this paper are those calculated over six strata. Confidence intervals were calculated as described by Rothman and Boice (*9*). Tests for significance of trend used the Mantel extension test (*10*). Pairwise correlations were calculated for the primary nutrition indices (*11*).

In general, controls with nutrition-related causes of death were not excluded from the dietary analyses. Nearly all major causes of death are believed to be associated with one dietary pattern or another, and selective exclusion might well compromise the broad representativeness of the control series. Relative weight, however, was analyzed with and without exclusion of obesity-related deaths from the control series.

RESULTS

The RR of esophageal cancer by consumption of the 31 individual food items are shown in table 1. RR tended to increase with decreasing consumption of beef, chicken, lamb, fresh or frozen fish, eggs, butter or margarine, fruit (excluding citrus fruit), bananas, leafy green vegetables, other green vegetables, and yellow vegetables (excluding corn). The RR tended to decrease with decreasing consumption of bacon, sausage, frank-

TABLE 1.—*RR of esophageal cancer by consumption of specific foods*

Food item	RR by consumption level[a]		
	High	Moderate	Low
1. Beef or veal	1.0	1.3	1.5
2. Chicken	1.0	1.0	1.3
3. Lamb	1.0	3.0	3.0‡
4. Ham or pork	1.0	1.5	1.0
5. Bacon	1.0	0.6	0.7*
6. Sausage	1.0	0.8	0.4†
7. Frankfurters	1.0	0.9	0.9
8. Lunch meat, e.g., salami, bologna	1.0	0.7	0.8
9. Corned beef or pastrami	1.0	1.0	1.0
10. Canned meat, e.g., Spam, Treet	1.0	0.7	0.6*
11. Liver	1.0	0.7	0.8
12. Brains or chitterlings (intestines)	1.0	1.3	1.0
13. Shellfish	1.0	1.5	0.8
14. Canned fish, e.g., tuna, sardines	1.0	0.9	0.4‡
15. Fresh or frozen fish, e.g., flounder, catfish	1.0	1.5	1.7
16. Eggs	1.0	1.3	1.5*
17. Cheese	1.0	1.3	0.9
18. Milk	1.0	1.7	1.4
19. Butter or margarine	1.0	1.0	1.2
20. Leafy green vegetables, e.g., spinach, kale	1.0	1.3	1.6*
21. Other green vegetables	1.0	1.2	1.3
22. Corn	1.0	1.0	0.9
23. Other yellow vegetables, e.g., carrots, squash	1.0	1.3	1.9†
24. Citrus fruits or juices	1.0	1.6	1.2
25. Bananas	1.0	1.8	1.7†
26. Other fruits, e.g., peaches, pears	1.0	1.4	2.5‡
27. Whole grain breads or cereals	1.0	1.2	1.1
28. Cornbread, corn mush, corn grits, etc.	1.0	1.1	0.9
29. Potatoes	1.0	1.1	0.7
30. Potato chips, fried potatoes, or fried onions	1.0	1.4	1.0
31. Peanuts or peanut butter	1.0	1.4	0.9

[a] Statistical significance of trend: *, $P<0.10$; †, $P<0.05$; ‡, $P<0.01$.

furters, lunch meat, canned meat, liver, canned fish, and potatoes. Adjusting the RR for the individual food items for ethanol consumption did not markedly alter them.

The RR of esophageal cancer by consumption of various food groups and micronutrients are shown in table 2. The ethanol-adjusted RR increased with decreasing consumption of dairy products and eggs, fruits and vegetables, vegetables alone, and fruits alone but were not markedly associated with carbohydrate or bread consumption. Nor was there a clear trend with total meat and fish consumption. However, the ethanol-adjusted RR increased with decreasing consumption of fresh or frozen meat and fish and tended to decrease slightly with decreasing consumption of precooked or processed meat and fish. The fresh or frozen meat and fish group, relative to the precooked or processed meat and fish group, contains foods that tend to be more expensive, more typical of an affluent diet, less processed, and less easily prepared. Although precooked or processed meat and fish consumption was slightly associated with esophageal cancer, consumption of nitrite-containing meats was not associated. Adjusting each of the food group and micronutrient RR for ethanol consumption produced no striking changes, as shown in table 2, nor did adjustment for cigarette smoking.

For fresh or frozen meat and fish, dairy products and eggs, and fruits and vegetables, the RR associated with low consumption was about twice that for high consumption. The approximate third of the study subjects who were categorized as low consumers of fresh or frozen meat and fish had 1-3 servings a week; the third categorized as high consumers had 6-18 servings a week. Low dairy product and egg consumption was 0-7 servings a week; high was 14-28 servings a week. Low fruit and vegetable consumption was 1-12 servings a week, and high was 20-43 servings a week. The ethanol-adjusted trends in RR for the three food groups were statistically significant and of similar magnitude. However, when consumption was divided into six levels rather than three, fresh or frozen meat and fish showed the clearest dose-response relationship, with the ethanol-adjusted RR of those with the lowest intake being 3.3, relative to those with the highest intake.

Risk was elevated among individuals with a low intake of vitamin A but there was no clear gradient; and the risk was less than that for low consumption of dairy products and eggs or fruits and vegetables, which are the major sources of vitamin A. Similarly, risk was elevated among those with a low intake of vitamin C or carotene; but the risk was somewhat less than that for low consumption of fruits and vegetables, the food group that provides vitamin C and carotene. Risk was elevated among those with a low intake of riboflavin, but not as markedly as among those with low consumption of dairy products and eggs, the major sources of riboflavin.

Esophageal cancer was also associated with two

TABLE 2.—*RR of esophageal cancer by consumption of food groups and micronutrients*

Nutrition index[a]	RR by consumption level[c]			RR adjusted for ethanol, by consumption level[c]		
	High	Moderate	Low	High	Moderate	Low
Food groups[b]						
Meat, fish, eggs, and cheese (1–17)	1.0	1.7	1.1	1.0	1.7	1.3
Meat and fish (1–15)	1.0	1.3	0.9	1.0	1.3	1.2
Dairy products and eggs (16–18)	1.0	1.6	2.0†	1.0	1.7	1.9†
Fruits and vegetables (20–26)	1.0	2.1	2.4‡	1.0	1.7	2.0†
Vegetables (20–23)	1.0	1.7	1.8†	1.0	1.5	1.6*
Green vegetables (20, 21)	1.0	1.2	1.5*	1.0	1.0	1.3
Yellow vegetables (22, 23)	1.0	1.0	1.2	1.0	1.0	1.7
Fruits (24–26)	1.0	2.8	2.4‡	1.0	2.4	2.0†
Carbohydrates (22, 27–30)	1.0	1.1	1.2	1.0	1.1	1.2
Bread (27, 28)	1.0	1.1	1.2	1.0	1.1	1.1
Fresh or frozen meat and fish (1–3, 13, 15)	1.0	1.5	2.1†	1.0	1.6	2.2†
Precooked or processed meat and fish (5–8, 10, 14)	1.0	0.9	0.8	1.0	0.9	0.9
Nitrite-containing foods (5, 7–10)	1.0	1.1	0.8	1.0	1.1	1.0
Micronutrients						
Vitamin A	1.0	1.4	1.5	1.0	1.5	1.5
Carotene	1.0	1.4	1.6*	1.0	1.3	1.3
Vitamin C	1.0	1.3	2.1‡	1.0	1.2	1.8†
Thiamin	1.0	1.2	1.1	1.0	1.2	1.2
Riboflavin	1.0	1.1	1.6*	1.0	1.0	1.7†

[a] Includes all food groups and micronutrients analyzed.
[b] Specific food items combined to form each food group are indicated by the *numbers in parentheses*, which refer to table 1.
[c] Statistical significance of trend: *, $P<0.10$; †, $P<0.05$; ‡, $P<0.01$.

TABLE 3.—*RR of esophageal cancer by relative weight*

Relative weight	No. of cases (% of all cases)	No. of controls (% of all controls)	RR[a] (95% confidence interval)	RR, excluding obesity-related deaths from controls[a] (95% confidence interval)
Light	13 (11)	19 (8)	1.2 (0.5–2.6)	0.9 (0.4–2.1)
Ideal	32 (28)	52 (22)	1.1 (0.6–1.9)	1.1 (0.6–2.1)
Typical	55 (48)	99 (42)	1.0	1.0
Heavy	15 (13)	64 (27)	0.4 (0.2–0.8)	0.6 (0.3–1.2)

[a] All risks relative to those of typical relative weight.

indirect measures of diet. Relative weight (wt/ht^2) was inversely related to risk, with the RR of the lightest third of the study sample being 2.4 that of the heaviest third ($P<0.01$, for trend). The ethanol-adjusted RR was 2.1. The number of meals usually eaten per day was also inversely related to risk, with those eating two meals a day (51 cases, 78 controls) having 1.8 times the risk of those eating three or more meals a day (55, 147, respectively) and those eating one meal a day (8, 9, respectively) having a risk of 2.4 relative to the same group ($P<0.01$, for trend). The ethanol-adjusted RR were 1.6 and 1.7, respectively. Adjustment for cigarette smoking did not markedly change these RR.

The RR for fresh or frozen meat and fish consumption, fruit and vegetable consumption, dairy product and egg consumption, usual number of meals eaten per day, and relative weight were controlled for socioeconomic status, as measured by education, and were not markedly changed. These results are shown in (*1*). The RR associated with less than 8 years of school, relative to 12 or more years, was 1.5, less than the risk associated with poor nutrition measured by any of the five nutrition indices. Occupation, another possible measure of socioeconomic status, was not related to esophageal cancer in this study (*1*).

The inverse association of esophageal cancer with relative weight was further examined by grouping the study subjects into four categories: those lighter than ideal, those close to the ideal relative weight, those close to the typical or median relative weight, and those heavier than typical. Table 3 shows that a slightly higher percentage of cases than controls were in each of the two lighter categories, but only 11% of the cases were actually in the lightest category. In comparison, 15% of U.S. blacks, 55–64 years of age, had relative weights in this range in the 1971–74 U.S. Health and Nutrition Examination Survey (Abraham S: Personal communication). There was only a small RR, about 1.2, for those especially light in weight relative to those of typical weight; but the RR for those who were especially heavy was 0.4. This reduced RR remained after exclusion of the 95 controls who died of obesity-related diseases (myocardial infarction, hypertensive heart disease, and diabetes). Adjustment for ethanol consumption did not change the pattern.

Table 4 shows the interrelationships among the five primary measures of nutritional status and ethanol consumption. The nutrition indices were positively, but weakly, correlated with each other. Thus there was sufficient variety of diet within the study population to allow each nutrition index to be adjusted for the others. When the ethanol-adjusted RR for fresh or frozen meat and fish consumption, fruit and vegetable consumption, and dairy product and egg consumption were adjusted for each other, separate effects for all three were evident. The ethanol-adjusted RR for fresh or frozen meat and fish consumption were the only RR for consumption of a food group to remain unchanged after controlling for consumption of another food group, with the RR of the low consumers, relative to high consumers, remaining about 2.2. Controlling the ethanol-adjusted RR for fruit and vegetable consumption or dairy product and egg consumption for another food group reduced the gradients, with the risk of the low consumers, relative to high consumers, falling from about 2.0 to about 1.6.

Fresh or frozen meat and fish consumption, fruit and vegetable consumption, and dairy product and egg consumption seemed to be relatively independent measures of dietary patterns, all similarly related to the risk of esophageal cancer. The ethanol-adjusted RR of individuals with low intake of two of the food groups was generally four times the risk of those with high intake of the same two food groups: the RR were 4.2, 3.9, or 2.8, depending on the pair of food groups being considered. The three food group consumption measures were then combined into a single measure of overall nutritional status. The RR for combinations of high, moderate, and low consumption of the three food groups are shown in table 5. The risk of esophageal

TABLE 4.—*Correlation matrix for the five primary nutrition indices and ethanol consumption*

Nutrition index	Fresh or frozen meat and fish	Fruits and vegetables	Dairy products and eggs	Relative weight	Meals/day	Ethanol, g
Fresh or frozen meat and fish	1.0	0.26	0.18	0.02	0.06	0.06
Fruits and vegetables		1.0	0.40	0.10	0.24	−0.13
Dairy products and eggs			1.0	0.04	0.21	0.00
Relative weight				1.0	0.13	−0.09
Meals/day					1.0	−0.26
Ethanol, g						1.0

TABLE 5.—*RR of esophageal cancer by an overall measure of food consumption patterns*

Food consumption pattern[a]	No. of cases	No. of controls	RR[b] (95% confidence interval)	RR, adjusted for ethanol[b,c]
HHH	2	20	1.0	1.0
HHM HMM	24	65	3.7 (0.8–17.0)	3.8
HHL MMM HML HLL	32	68	4.7 (1.0–21.4)	4.5
MML MLL	36	46	7.8 (1.7–35.7)	6.7
LLL	11	8	13.8 (2.5–76.4)	15.0

[a] Concurrent level of consumption of fresh or frozen meat and fish, fruits and vegetables, and dairy products and eggs, each rated as high (H), moderate (M), or low (L). For example, HML indicates high consumption of 1 of the 3 food groups, moderate consumption of a 2d, and low consumption of a 3d.
[b] All risks relative to those consuming high quantities of all 3 food groups (HHH).
[c] The categories of ethanol consumption were 0–5.9 and 6.0–80.0 fl oz of hard liquor equivalents/day.

cancer decreased steadily with improving patterns of food consumption. Relative to those who consumed high quantities of all three food groups (HHH), those who consumed low quantities of all three (LLL) had 14 times the risk. Adjustment for ethanol, across only two strata because of sparse numbers in the extreme nutrition categories, did not reveal any confounding, as shown in table 5.

With this overall measure of food consumption patterns as the nutrition index, the interaction of nutritional status and ethanol intake was examined. As shown in table 6, the risks for poor nutrition and ethanol intake remained distinct and seemed to be multiplicative. With different divisions of the nutrition and ethanol variables or different nutrition indices, other patterns emerged, with combined effects often being less than multiplicative. Nonetheless, the elevated risk associated with poor nutrition could be detected across each level of ethanol consumption considered. It was not possible to determine whether poor nutrition was a risk factor among those unexposed to ethanol, since only 5 cases did not drink.

Beer, wine, and hard liquor provide almost none of the daily requirements for micronutrients and protein and therefore can be considered empty calories. Alcoholic beverage intake for the study subjects was converted to empty calorie intake and related to the risk of esophageal cancer, as shown in table 7. The RR rose steadily from 1.0 to 4.1 to 6.4 as the percent of the estimated caloric need of the average adult male, 51-75 years of age, that was being supplied by alcoholic beverages rose from less than 0.03% to 0.03-20% to 21-80%. When each study subject's intake of empty calories was divided by his usual adult weight, the gradient in RR became somewhat smoother. Dividing intake of empty calories by height produced similar results.

Information was collected on whether the usual method of cooking meat and fish was frying, baking, broiling, or a combination. Most of the study population (51%) fried their meat, and most (83%) fried their fish. The RR dropped to 0.6 (95% confidence interval = 0.3-1.1) when meat was usually baked rather than fried and to 0.3 (0.2-0.7) when meat was usually broiled. Those who usually baked or broiled fish rather than fried it showed similarly reduced RR of 0.8 (0.3-2.3) and 0.2 (0.1-0.6), respectively, although the numbers were sparse. These associations of esophageal cancer with the cooking method were not markedly reduced when adjusted for ethanol consumption, fresh or frozen meat and fish consumption, or education.

DISCUSSION

Poor nutrition is suspected to be a cause of esophageal cancer for several reasons. 1) In Iran (*12*), the Soviet Union (*13*), and China (*14*) esophageal cancer is endemic in regions with limited diets and impoverished agriculture. 2) Case-control studies in the United States (*15, 16*) and Iran (*17*) and a prospective cohort study in Japan (*18*) have demonstrated an association between reduced consumption of certain basic food groups, notably vegetables and fruits, and esophageal cancer. These studies, as well as case-control studies in Puerto Rico (*19*) and Singapore (*20*), have also shown an association between low socioeconomic status and esophageal cancer. 3) Within the United States mortality rates for esophageal cancer are inversely related to county socioeconomic indices and are higher among blacks than whites (*21*). 4) Until recently, esophageal

TABLE 6.—*RR of esophageal cancer by nutritional status and ethanol consumption*

Ethanol consumption, in hard liquor equivalents	Nutritional status[a]		
	High	Moderate	Low
0–5.9 fl oz/day	1.0[b] (6, 43)[c]	1.7 (6, 25)	3.0 (8, 19)
6.0–80.0 fl oz/day	2.7 (13, 34)	4.1 (21, 37)	8.0 (29, 26)

[a] Concurrent level of consumption of fresh or frozen meat and fish, fruits and vegetables, and dairy products and eggs. High, moderate, and low nutritional status were defined as food consumption patterns HHH, HHM, and HMM; patterns HHL, MMM, HML, and HLL; and patterns MML, MLL, and LLL, respectively.
[b] All risks relative to those who drank <6 fl oz/day and were of high nutritional status.
[c] *Numbers in parentheses* are numbers of cases and controls. Excluded from analysis were those of unknown nutritional status or with unknown ethanol intake.

TABLE 7.—*RR of esophageal cancer by consumption of the empty calories in alcoholic beverages*

kcal of beer, wine, and hard liquor consumed weekly	Percent of caloric needs filled by alcoholic beverages[a]	No. of cases	No. of controls	RR by empty calories[b] (95% confidence interval)	RR by empty calories/weight[b,c] (95% confidence interval)
<500	<0.03	5	55	1.0	1.0
500–3,360	0.03–20	16	43	4.1 (1.4, 12.1)	4.5 (1.5, 13.2)
3,361–6,720	21–40	18	31	6.4 (2.1, 18.8)	5.6 (1.9, 16.2)
6,721–13,440	41–80	28	49	6.3 (2.3, 17.6)	6.4 (2.3, 18.2)
>13,440	>80	23	35	7.2 (2.5, 20.8)	7.1 (2.5, 20.4)

[a] Daily caloric need of each individual was assumed to be 2,400 kcal, on the basis of the National Academy of Sciences' recommendation for U.S. males, 51–75 yr of age (*5*).

[b] All risks relative to those who drank <500 kcal of beer, wine, or hard liquor/wk.

[c] Empty calories/weight was cut into strata that were almost identical in size to those chosen for empty calories.

cancer was unusually common in women from the rural, northern areas of Sweden, many of whom also had the Plummer-Vinson (or Paterson-Kelly) syndrome, which is associated with iron and other micronutrient deficiencies (*22, 23*). 5) Esophageal cancer has been reported as a sequel of celiac disease, a malabsorption disorder of the small intestine (*24, 25*).

Several micronutrients can be postulated to play a role in the etiology of esophageal cancer. In experimental animals very large doses of analogs of vitamin A have been shown to protect against the development of cancer, whereas vitamin A deficiency often increases the risk (*26*). Either dietary vitamin A or dietary carotene could be the protective agent. Vitamin C is known to block the formation of N-nitroso compounds (*27*), carcinogens that can be formed in food or in the digestive tract once nitrite is present. Riboflavin, niacin, and vitamin B_6 are all essential for the health and integrity of the epithelium, particularly along the upper digestive tract (*28*). Thiamin deficiency is common among chronic alcoholics, and iron deficiency appears to be partly responsible for the Plummer-Vinson syndrome (*22*).

In this case-control study of an urban black male population with strikingly high mortality from esophageal cancer, poor nutrition was identified as a primary risk factor. Consumption levels of fresh or frozen meat and fish (beef, chicken, lamb, fish, shellfish), fruits and vegetables, and dairy products and eggs were inversely associated with esophageal cancer. For each of these measures of food group consumption, there were statistically significant trends in RR, with the least nourished third of the study population having twice the risk of the most nourished third. Individuals who consumed low levels of any two of these three specific food groups had about four times the risk of those who consumed high levels of the same two food groups. When the three food group consumption measures were combined into a single comprehensive nutrition index, the RR between extremes was 14, with a 95% confidence interval of 2.5-76. In addition, there were statistically significant inverse trends in RR, with gradients around twofold, for two indirect measures of nutritional status: relative weight (wt/ht^2) and number of meals eaten per day. All of these nutrition-related RR are adjusted for ethanol consumption.

The association of esophageal cancer with poor nutrition appeared to be independent of any associations with alcohol consumption (the other major risk factor in these urban black men), with smoking, or with socioeconomic status. Adjustment for these potential confounders did not markedly change the relationships between the various nutrition measures and esophageal cancer risk; and the associations were consistently seen across the various levels of ethanol consumption, smoking, and socioeconomic status. Because the association of esophageal cancer with poor nutrition was independent of socioeconomic status, it seems unlikely that unidentified aspects of life-style, correlated with dietary patterns, are primarily responsible.

Before interpreting these associations between diet and esophageal cancer, it is necessary to assess their validity. Esophageal cancer might restrict food consumption through dysphagia or anorexia and thus influence the dietary history of the cases. Therefore, in this study next of kin were deliberately asked about the subjects' usual adult diet several years prior to death. The specificity of the associations that emerged suggests that the disease process itself did not create the differences in dietary patterns between cases and controls nor did it bias the recall of diet by the next of kin. Although consumption of 11 food items decreased with increasing risk, consumption of 8 other food items increased with increasing risk; and no association was seen for consumption of the other 12 food items. As for the food groups, cases were reported to eat significantly less fresh or frozen meat and fish, fewer fruits and vegetables, and fewer dairy products and eggs than the controls but similar amounts of carbohydrates and precooked or processed meat and fish. Thus consumption of a few food groups, typically associated with a sensible diet, was selectively reduced. In addition, the usual adult weight, several years prior to death, recalled by the next of kin, indicated a smaller percentage of very light individuals among the cases than that reported for blacks of similar age in the 1971-74 U.S. Health and Nutrition Examination Survey. Thus there is no suggestion of a general decrease in total food consumption among the cases, which might have resulted from preclinical cancer.

Information on dietary patterns is occasionally criticized as imprecise and of limited value, especially if obtained from next of kin. However, in this study relatively strong associations with clear gradients were repeatedly noted; and the relationship that emerged was internally consistent. First of all, poor nutrition, whether measured by consumption of certain specific food groups, anthropometry, or frequency of eating, was repeatedly associated with increased risk of esophageal cancer. Second, similar food items, such as the various individual fruits and vegetables, were similarly associated with risk. Random misclassification of exposure might obscure a true association, but it does not generate a false association.

To help evaluate the validity and reliability of the next of kin responses, the RR for several of the nutrition measures were calculated separately for interviews of wives and of other next of kin. They were generally comparable. For example, for the general measure of nutritional status defined in table 6, the RR rose, as nutrition declined, from 1.0 to 1.4 and 3.0 among the subjects whose wives were interviewed and from 1.0 to 1.7 and 2.8 among the other subjects.

The relationships identified in this study suggest that general malnutrition, probably of a mild form, increases the susceptibility of urban black men to esophageal cancer. No direct evidence for a specific nutritional deficiency was found. Estimates of the intake of vitamin A, carotene, vitamin C, thiamin, and riboflavin were each less strongly associated with esophageal cancer than was consumption of the basic food groups that provide most of each micronutrient. In addition, the micronutrient indices were not as strongly associated as such general measures of nutritional status as relative weight and meals eaten per day. However, the micronutrient estimates were constrained by the food frequencies actually asked in the interview. For example, no information on tomato consumption could be incorporated into the vitamin C estimates; and no information on fortified bread and cereal consumption could be incorporated into the thiamin and riboflavin estimates. A niacin index was not formed because of the difficulty of estimating the contribution of tryptophan intake (*5*), and an iron index was not formed because of uncertainty about the degree of absorption of iron in different foods and at different meals (*29*).

Consumption of bacon, frankfurters, lunch meats, and canned meats was more frequent among the cases than the controls and suggested exposure to nitrites and possible formation of endogenous N-nitroso compounds. However, canned fish, which contains no nitrite, and breakfast sausage, which usually contains no nitrite either, were also consumed more frequently by the cases. Thus esophageal cancer seemed more closely associated with precooked or processed meat and fish consumption than with nitrite intake.

The inverse association with relative weight resulted primarily from a reduced risk among heavy individuals. The RR for heavy subjects was approximately half that for those of typical weight. Risk was not markedly elevated among light subjects. It is plausible that in this study population, with its high intake of alcoholic beverages and the resultant empty calories, only those who regularly consumed more than their daily caloric needs and thus maintained excess weight were able to approach reasonable intakes of a variety of nutritious food groups.

The mechanism by which alcohol increases the risk of esophageal cancer is not known, and attempts to produce cancer in well-nourished laboratory animals by prolonged ingestion of ethanol have failed (*30*). Since poor nutrition is a risk factor for esophageal cancer, it is conceivable that alcohol increases risk, in part, by reducing nutrient intake. Beer, wine, and hard liquor provide a share of the daily caloric needs and consequently reduce appetite but provide almost none of the daily requirements for micronutrients and protein. In this study the risk of esophageal cancer increased sharply with heavy consumption of alcoholic beverages, whether measured as intake of empty calories or grams of ethanol.

Among these urban black men the risk of esophageal cancer associated with alcoholic beverage consumption seemed relatively independent of the association with poor nutrition. Alcohol consumption was only weakly correlated with the primary nutrition indices. Nonetheless, it is possible that alcohol consumption functions by a nutritional mechanism. Alcohol intake could be a partial measure of the underlying dietary determinants of esophageal cancer in much the same way as fresh or frozen meat and fish consumption and fruit and vegetable consumption are only partially correlated with each other, and yet each partially measures overall nutritional status and the related risk of esophageal cancer.

The usual method of cooking was also related to risk of esophageal cancer. Those who usually baked or broiled meat or fish were at less risk than those who usually fried meat and fish. Cooking practices are often influenced by the type of foods purchased. In this study population, however, the usual method of cooking was not consistently correlated with consumption of either the fresh or frozen or the precooked or processed meat and fish groups. The implications of the risk associated with frying foods are not clear and suggest further study.

This study was unable to identify a specific nutritional deficiency associated with the high risk of esophageal cancer among urban black men. However, a provocative pattern of generally poor nutrition was clearly associated with risk; a complex nutritional deficiency, involving several micronutrients or food groups, may be involved. A precedent exists for this hypothesis since many of the nutritional deficiencies observed in humans, such as protein-calorie malnutrition, encompass multiple inadequacies (*31*).

The nutrition-related associations identified in this study were relatively strong, graded with respect to exposure level, internally consistent, and specific, all of which was reassuring in view of the difficulties inherent in the study design. Information on usual diet several years earlier was obtained from next of kin, and occasionally close friends, for persons who often had limited education, histories of heavy drinking, and thus presumably erratic life-styles. Future studies involving a large number of study subjects and more detailed and varied questions about diet might narrow the associations indicated by this study and further clarify the role of nutrition in the development of esophageal cancer.

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